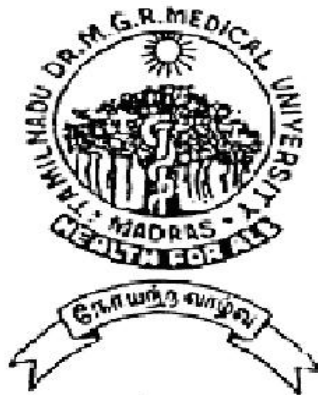


**BACTERIOLOGICAL PROFILE AND THEIR
SENSITIVITY PATTERN
IN LEUKEMIC PATIENTS**

Dissertation Submitted for

MD Degree (Branch VII) PEDIATRICS

April 2011



The Tamilnadu Dr.M.G.R.Medical University

Chennai – 600 032.

MADURAI MEDICAL COLLEGE, MADURAI.

CERTIFICATE

This is to certify that this dissertation titled “**BACTERIOLOGICAL PROFILE AND THEIR SENSITIVITY PATTERN IN LEUKEMIC PATIENTS**” submitted by **DR.V.SANKAR** to the faculty of Pediatrics, The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD Degree Branch VII Pediatrics, is a bonafide research work carried out by him under our direct supervision and guidance.

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INTRODUCTION

Leukemia is the most common cancer among children in world. It is the commonest cause of mortality and morbidity among all cancers. Among all causes infection is the most common cause of mortality and morbidity among leukemic patients.

Statement of problem and need of the study

As with any immune compromised child, leukemic children are more prone for various types of infections. It is an universal problem even in developed nations with highly sterilized aseptic wards. Hence, this being an important problem, I had decided to take up this study of analysing the common organisms and their sensitivity in leukemic patients.

Leukemic patients experience recurrent febrile episodes during the course of their disease. This is because leukemic patients are more prone for recurrent opportunistic infections due to immunosuppression and neutropenia caused by chemotherapy and the disease per se¹. But only limited data is available regarding the changing pattern of infections and their sensitivity to antibiotics from South Tamilnadu.

The present study, therefore, was planned to study the infections in leukemia patients with reference to the causative organism and the culture sensitivity pattern of these organisms at the INSTITUTE OF CHILD HEALTH, MADURAI for a period of TWO years.

Leukemia

It is defined as the group of malignant diseases in which genetic abnormalities in a hemotopoietic cell gives rise to a clonal proliferation of cells resulting in disruption of normal marrow function and ultimately marrow failure². Healthy bone marrow makes blood cells that stop bleeding and fight infections. In leukemia, bone marrow makes abnormal blood cells that are unable to do this critical job.

Symptoms of Leukemia

Initial presentation of ALL is usually non specific. Anorexia, fatigue, irritability, intermittent fever are initial symptoms. Bone / joint pain may be present. As the disease progress signs of bone marrow failure like pallor, fatigue, bruising (or) epistaxis as well as fever which may be caused by infections appear³.

On examination pallor, listlessness, purpura, petechial skin lesions (or) mucus membrane hemorrhage may occur. The proliferative

nature of leukemia manifests as lymphadenopathy, splenomegaly and hepatomegaly⁴.

Types of leukemia

Acute Lymphoblastic Leukemia is the most common type of leukemia in children (77%). Next is Acute Myelogenous Leukemia which is about 11% followed by chronic myelogenous leukemia (3-5%). Rest of 7-9% cases include a variety of acute and chronic cases that do not fit classic definitions of above⁵.

Leukemia is commonly treated with chemotherapy and radiotherapy.

Frequent infections in leukemia

Leukemia can make the body extremely vulnerable to infection, which may seem confusing because of increased numbers of white blood cells. Unfortunately, the abnormal white blood cells that are produced do not have the ability to effectively fight against infections and there are not usually enough healthy white blood cells to keep the immune system strong. In the post chemotherapy scenario where the patients are in a state of bone marrow depression they are also vulnerable to infections due to neutropenia.

Fever is one response of the immune system to infections and are caused by the release of chemicals that tell the brain to raise the body's temperature. When a person has leukemia, these chemicals may be released excessively, causing frequent or persistent fevers mostly caused by infections.

Although fever can be induced by other causes such as blood products, drugs or thrombophlebitis, fever in neutropenic host must be considered as a potential sign of infection. The infections caused by bacteria, viruses, fungi and parasites are the common cause of morbidity and mortality.

It has been pointed out for more than 30 years that the risk of infection increases with the 'degree and duration of neutropenia'. Cytotoxic regimens used for malignancies may produce neutropenic episodes ($ANC < 0.5 \times 10^9/l$) of either short duration, i.e. less than 7 - 10 days, or more prolonged (2-3weeks). Infections of skin, soft tissue GI tract, bacteremia are more common in leukemics. The natural commensals can invade the host to produce symptoms due to immunocompromised state. Cytotoxic drugs preferentially affects myeloid cells and are the common cause of neutropenia. Its incidence increases with age of the patient.

Neutropenia

It is defined as an absolute neutrophil count (ANC) of less than 1500/ μ L. The ANC is equal to the product of the white blood cell count (WBC) and the percentage of polymorphonuclear cells (PMNs) and band forms noted on the differential analysis:

$$\text{ANC} = \text{WBC (cells}/\mu\text{L)} \times \text{percent (PMNs + bands)} \div 100$$

Neutrophilic metamyelocytes and younger forms are not included in this calculation. The risk of infection begins to increase at an ANC below 1000/ μ L.

Neutropenia, is a hematological disorder characterized by an abnormally low number of neutrophils, the most important type of white blood cell, in the blood. Neutrophils usually make up 50-70% of circulating white blood cells and serve as the primary defense against infections by destroying bacteria in the blood. Hence, patients with neutropenia are more susceptible to bacterial infections and, without prompt medical attention, the condition may become life-threatening (neutropenic sepsis).

Neutropenia can be acute or chronic depending on the duration of the illness. A patient has chronic neutropenia if the condition lasts for longer than 3 months. Some common symptoms of neutropenia

include fever and frequent infections. These infections can result in conditions such as mouth ulcers, diarrhoea, a burning sensation when urinating, unusual redness, pain, or swelling around a wound, or a sore throat.

A complete blood count (CBC), detects neutropenia. Fortunately, neutropenia is easily prevented or reduced by granulocyte – colony stimulating factor (pegfilgrastim or filgrastim, the short-acting form). These medications help to produce more white blood cells and prevent the complications of neutropenia.

It is given with the first cycle of chemotherapy after 15 days of starting the chemotherapy and then with each remaining chemotherapy cycle. This can reduce the risk of infection (neutropenia with fever) by more than 90 percent.

Candidiasis, invasive fungal infections [aspergillosis] and viral infections [herpes] are common in leukemics. They are empirically treated with fluconazole, amphotericin and acyclovir respectively.

An opportunistic infection is an infection caused by pathogens (bacterial, viral, fungal or protozoal) that usually do not cause disease in a healthy host, i.e. one with a healthy immune system.

A compromised immune system, however, presents an "opportunity" for the pathogen to infect.

Approach for the diagnosis of infection

1. Sample/ swab was obtained
2. The specimen is gram-stained. The shape, size, arrangement and whether they are gram-positive or gram-negative should be observed.
3. The specimen is cultured on appropriate media, to obtain 'pure culture'. Plates should be incubated in aerobic or anaerobic environment.
4. Perform antibiotic susceptibility tests.

Blood culture

A minimum of 1:10 of blood: culture is taken through venipuncture and injected into two or more bottles with specific media for aerobic organisms.

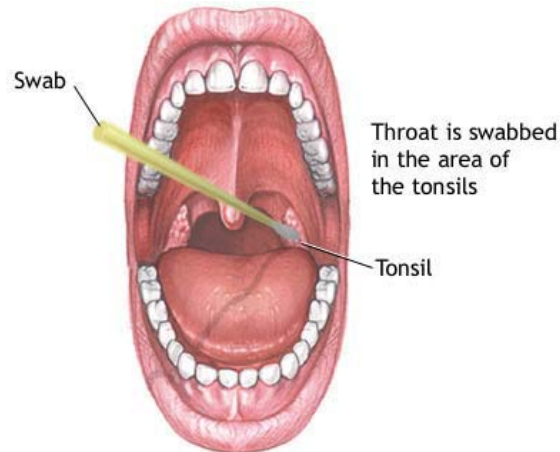
The blood is collected using clean technique. This requires that both the tops of the culture bottles and the venepuncture site of the patient are cleaned prior to collection. Microbiological cultures utilize petri dishes of differing sizes that have a thin layer of agar based

growth medium in them. Once the growth medium in the petri dish is inoculated with the desired bacteria, the plates are incubated in an oven usually set at 37 degrees Celsius.

Another method of bacterial culture is liquid culture, in which case desired bacteria are suspended in liquid broth, a nutrient medium. These are ideal for preparation of an antimicrobial assay. The experimenter would inoculate liquid broth with bacteria and let it grow overnight in a shaker for uniform growth, then take aliquots of the sample to test for the antimicrobial activity of a specific drug or protein (antimicrobial peptides).

Procedure for throat swab collection

1. With the patient's head tilted back and the throat well illuminated, depress the tongue so that the back of the throat can be seen.
2. Rub the swab up and down the back of the throat and against any white patches in the tonsillar area. Avoid the tongue and the cheeks.
3. Replace the swab in the transport tube.
4. Seal tube tightly and Send the specimen to the laboratory



Skin wound swab collection

1. Using sterile gloves, thoroughly rinse the wound with normal saline to irrigate the excess debris and dirt.
2. Gently blot excess saline with sterile gauze.
3. After hand wash and sanitizing, use next pair of gloves and gently rotate the top of swab in wound without touching the edges.
4. Apply little pressure to get tissue fluid and put the swab in transport container and send it to laboratory.

Culture Media

A substance, either solid or liquid, used for the cultivation, isolation, identification, or storage of microorganisms.

A **culture** is any growth or cultivation of microorganisms. Cultivation is the process of inducing microbe to grow. The term

culture is usually employed for a deliberate growth in the laboratory.

Microbes are thus cultivated in vitro.

A **pure culture** is one that contains only a single kind (species) of microbe. To culture microbes in laboratory we require the preparation of substances which they can use as nutrients. Such nutrient preparations which microorganisms can use for growth are called culture media. Different microorganisms require different nutrient materials. Thus culture media vary in form and composition, depending on the species to be cultivated.

There are three main types of culture media: (i) Natural or empirical culture media, (ii) Synthetic or defined culture media, and (iii) Living media.

About 70% of all deaths in acute leukemic cases are attributed to infections^{3,11}. Moreover, there is a change in pattern of opportunistic infections in recent years^{4-5,13-15}. There are few reports on this aspect from different hospitals of India^{5,15-18}.

REVIEW OF LITERATURE

Infections in immune compromised patients like Leukemia is a major cause of mortality. Various micro organisms contribute to infection as host immunity is suppressed.

A similar study done by Gopalanath et al in Banaras Hindu University, Varanasi revealed a wide spectrum of infections in patients with absolute neutrophil count $<500^1$.

Leukemic patients are more prone to infections with pyogenic bacteria like pneumococci, streptococci, meningococci, pseudomonas and H.influenza^{2,30}.

Also gram negative septicaemia is more common leading to septic shock. These group can be differentiated into lactose fermenters, (commensals) and non-fermenters (pathogenic) by Mcconkey medium^{3-4,31}.

Staphylococcus and pseudomonas infection are severe and resistant to commonly used antibiotics^{4,32}.

Staphylococcus can be coagulase positive (S.Aureus) or coagulase negative (S.epidermidis, S.hemolyticus, S.Saprophyticus)^{5,33}.

Caselli et al⁶ in his study concluded pseudomonas resistance in immunocompromised undergoing chemotherapy as a major threat, which leads to increased mortality.

In a Pakistan study the most common opportunistic infections in leukemia are Tuberculosis, Candidiasis, Herpes zoster, hepatitis viruses, CMV, cryptococcus etc⁷.

Shawn Lockhart et al²³ concluded that pseudomonas aeruginosa, E.coli and klebsiella are the predominant organisms and imipenem as the single most effective antibiotic against them.

Novakova et al reported ceftazidime and imipenem for empirical treatment of febrile neutropenic patients²⁴.

Ashour et al study shows CONS and St.aureus as the most common gram positive bacteria²⁵.

Gram-positive pathogens have become a common cause of bacteraemia in granulocytopenic cancer patients. This has been partially attributed to the use of central intravenous devices such as Hickman catheters; mucositis secondary to intensive antineoplastic chemotherapy or herpes infections may also be the source, especially

for streptococci, whereas the skin is most probably the source for *Staphylococcus epidermidis*.

Antimicrobial prophylaxis recommended mainly with the aim of reducing the incidence of Gram-negative bacillary infections may also play a significant role. The rate of response of documented infections caused by Gram-positive cocci to 'standard' empirical therapy (which has been mainly directed against Gram-negative bacilli) has been unsatisfactory although the lethality reported has been low. These results raise an important question, whether or not a specific anti-Gram-positive antibiotic such as vancomycin, should be added to the empirical regimen⁸.

Viscoli et al⁸ described the increased incidence of such gram positive infections in leukemics.

Young et al¹⁹ concluded that cotrimoxazole prophylaxis decrease prevalence of most bacterial infections.

Maxwell Finland¹⁰ et al in his study also emphasised the changes patterns of susceptibility of common bacterial pathogens to antimicrobial agents in leukemics.

Hartstein et al²¹ even compared the antimicrobial susceptibility with plasmid profile analysis as identity tests.

Nosocomial infections pose significant threats to hospitalized patients, especially the immunocompromised ones, such as cancer patients. Ashour and Sheriff²⁵ in his study examined the microbial spectrum of gram-negative bacteria in various infection sites in patients with leukemia. The antimicrobial resistance patterns of the isolated bacteria were studied. The most frequently isolated gram-negative bacteria were *Klebsiella pneumonia* (31.2%) followed by *Escherichia coli* (22.2%).

Surveillance study by Liang et al²⁸ showed that significantly fewer bacterial stains were resistant to ofloxacin than to co-trimoxazole and that acquisition of resistance to co-trimoxazole was more commonly observed than was acquisition of resistance to ofloxacin. Significantly more patients had skin rashes following co-trimoxazole than ofloxacin treatment (P less than 0.05). Ofloxacin was superior to co-trimoxazole in preventing infection in this population of neutropenic patients.

Incidence of fungal infections were lower in leukemics in Indian studies^{15-18,20} but Choi²¹ and Riberio²² reported significant detectable rates abroad.

Infections commonly associated with neutropenia are bacterial (gram negative sepsis, pertusis, typhoid fever, disseminated tuberculosis, brucellosis), viral (measles, rubella, mumps, varicella, EBV, influenza, viral hepatitis, RSV, cytomegalovirus, HIV) protozoal (malaria, Leishmaniasis) fungal (Histoplasmosis) and rickettial.

Bone marrow infiltration with leukemic cells results in suppression of myelopoiesis leading to pancytopenia and leucocytosis in peripheral blood smear.

AIM OF THE STUDY

1. To Study the bacteriological profile (incidence of common bacterial pathogens) in leukemic children
2. To analyse the common antibiotic sensitivity patterns for these isolated organisms.

MATERIALS AND METHODS

This was a hospital based observational prospective study conducted in all leukemic children admitted in paediatric Hemato oncology ward, GRH, Madurai for a period of 2years (Oct 2008 to Oct 2010)

Settings :

This study is conducted in pediatric hematooncology ward in collaboration with the Department of Microbiology, GRH, Madurai.

Ethical Committee : Ethical clearance obtained from ethical committee Government Rajaji Hospital, Madurai.

Study Design : observational and analytical

Study Period : 2 Years

Inclusion Criteria :

All newly diagnosed and old cases of leukemic on chemotherapy <12years with symptoms / signs of infection admitted in Rajaji Hospital, Madurai

Methodology:

Data regarding the sex, age, symptoms, clinical profile, lab parameters, culture reports, antibiotic sensitivity were collected.

Febrile subjects were investigated for haemoglobin and counts of total leukocyte (TLC), differential leucocyte (DLC), platelet, absolute neutrophil (ANC). Swabs were taken from skin, oral cavity, nasal mucosa, catheter tips, venflon sites, throat, external ear etc. Blood, pus, urine, stool and CSF specimens were taken as per indication under full aseptic precautions. The specimens were processed by direct inoculation as well as enrichment on appropriate media.

Special care was taken in collecting blood sample for culture. The area to be pricked was thoroughly cleaned with spirit and povidone iodine. Sterile disposable syringes were used. The sample was then transferred to glucose broth media (1ml blood in 10ml media). After incubating for 24 hours at 37⁰C the sample was transferred into nutrient agar and McConkey media.

The organisms were allowed to grow in the plate at 37⁰C for 24 hours. After further processing of the colonies, the culture was

reported, results were obtained after 48 hours, sometime after 72 hours. Culture was reported as negative if there was no growth after 48 hours.

Samples were taken from every possible source of infection in febrile cases like blood, urine, throat pus & motion. A study of the sensitivity pattern of the organisms isolated to the drugs commonly available in our hospital was also conducted. The sensitivity pattern to ampicillin (AMP), gentamicin (GM), cotrimoxazole (CO), ciprofloxacin (CIP), cefotaxime (CEF), amikacin (AMIK), ceftriaxone (CEFTRI), doxycycline (DO) were reported.

RESULTS AND ANALYSIS

The results were analysed based on the culture reports and their sensitivity patterns. The commonest organisms isolated from these patients were identified from individual sites.

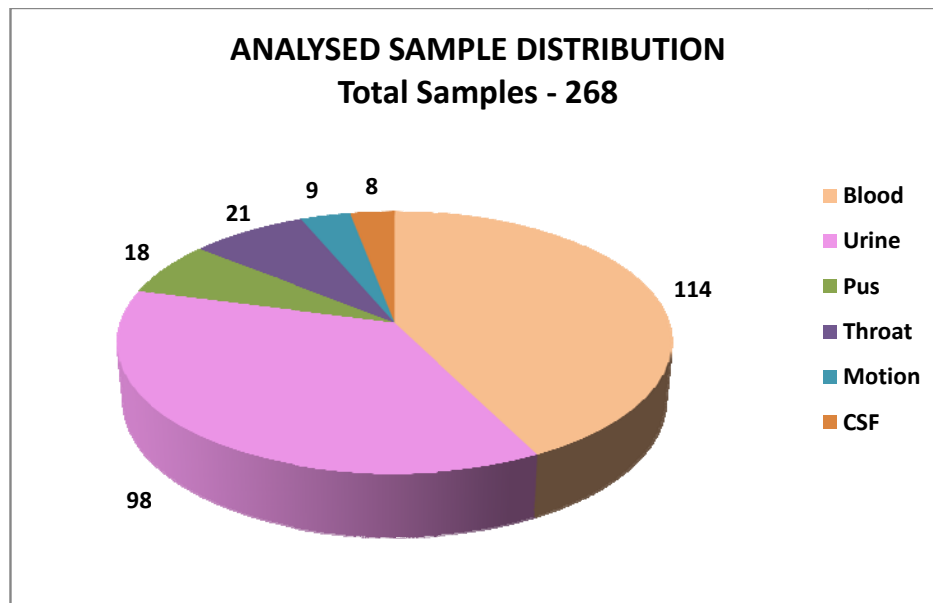
The total number of samples analysed for culture were 268. Blood (114) and urine (98) constitutes the major bulk of samples.

Pus, throat, motion and CSF constitute the remaining samples.

ANALYSIS OF SAMPLES

TOTAL NO OF SAMPLES SENT FOR CULTURE-268

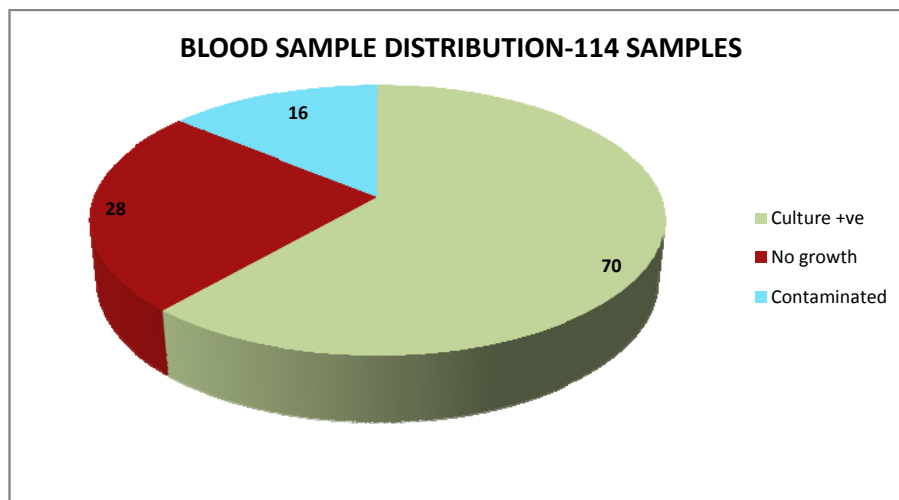
- Blood-114
- Urine-98
- Pus-18
- CSF-8
- Throat-21
- Motion-9



BLOOD CULTURE SAMPLES

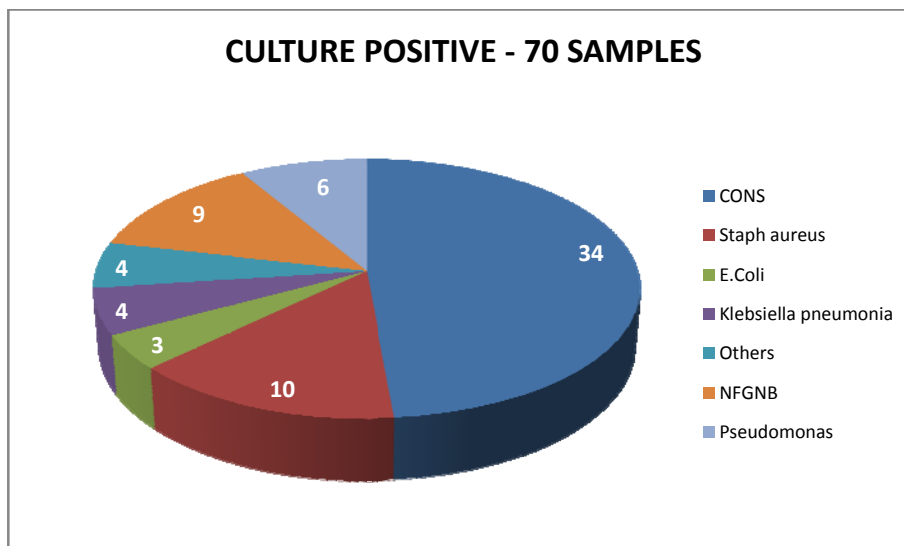
Total samples-114

- Culture +ve-70
- No growth-28
- Contaminated-7
- Aerobic spore bearers-4
- Skin commensals-5



BLOOD CULTURE POSITIVE – 70 SAMPLES

S.No	Organisms	No. of Culture	Percentage
1	CONS	34	48.51%
2	Staph aureus	10	14.28%
3	E.Coli	3	4.28%
4	Klebsiella pneumonia	4	5.71%
5	Klebsiella aerogens	1	1.43%
6	NFGNB	9	12.85%
7	Coliforms	1	1.43%
8	Pseudomonas	6	8.57%
9	Staphalbus	1	1.43%
10	Enterococcus	1	1.43%



BLOOD CULTURE AND ANTIBIOTICS SENSITIVITY

Total Number of Positive Samples – 70 Samples

ORGANISMS	AMP	GM	DO	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
CONS[34]	5	20	7	24	12	2	29	11	27	21
ECOLI[3]		1		3		2			3	3
KLEBSIELLA[5]		2		2	1			1	1	3
NFGNB(9)		3		4		1			1	6
ST.AUREUS[10]		1		4	1	1	6	1	1	3
PSEUDOMONAS[6]		2		3			2			4
COLIFORMS[1]		1				1			1	1
ENTEROCOCCUS[1]				1					1	1
STAPH.ALBUS	1				1		1			

Bacteriological profile of blood culture

CONS (34/70) was the commonest organism isolated from blood accounting for about 48.51% of positive culture.

Staphylococcus aureus (10/70) is the next common organism accounting for 14.27% of total positive cases.

NFGNB (9/70) accounts for 12.85% of positive samples. E.coli and klebsiella accounted for 10% of cases.

Other organisms grown were coliforms, enterococcus and staphylococcus albus.

Antibiotic sensitivity pattern

In blood culture CONS which was the predominant organism grown in blood culture was found to be susceptible to cloxacillin in 85.29% (29/34) of cases followed by ceftriaxone [79.4%] (27/34) and ciprofloxacin [70.59%] (24/34). Aminoglycosides (GM, amikacin) was sensitive in 60% (20/34) of cases.

Staphylococcus aureus was susceptible to cloxacillin in 60% of cases followed by ciprofloxacin (40%) and amikacin (30%).

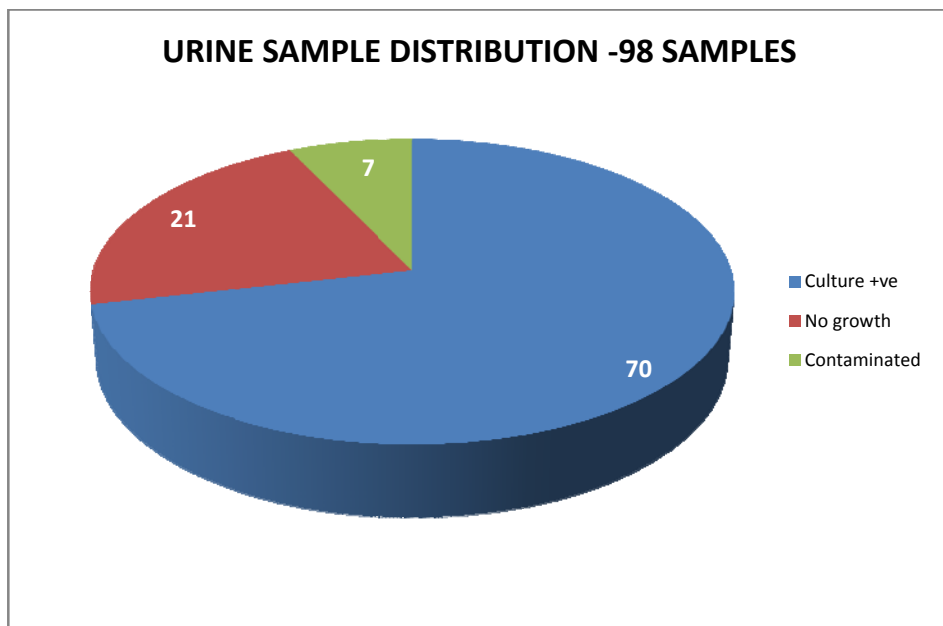
NFGNB is highly sensitive to amikacin (66%) followed by ciprofloxacin (45%) and gentamicin (34%).

Pseudomonas- Amikacin was the most effective antibiotic (66%) followed by ciprofloxacin (50%) gentamicin (33%) and cloxacillin (33%). Klebsiella – Amikacin is effective in 60% of cases followed by ciprofloxacin 40% and gentamicin 40%.

URINE CULTURE SAMPLES

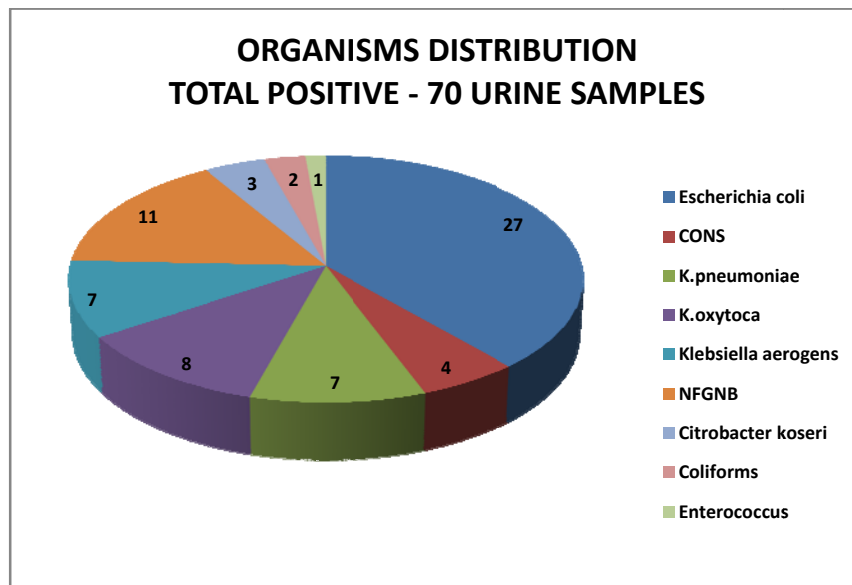
Total samples - 98

- Culture +ve - 70
- No growth - 21
- Contaminated - 7



Urine Culture +ve -70 Samples

S.No	Organisms	No. of Samples	Percentage
1	Escherichia coli	27	38.57%
2	CONS	4	5.71%
3	Klebsiella pneumoniae	7	10%
4	Klebsiella oxytoca	8	11.42%
5	Klebsiella aerogens	7	10%
6	NFGNB	11	15.71%
7	Citrobacter koseri	3	4.28%
8	Coliforms	2	2.85%
10	Enterococcus	1	1.43%



URINE CULTURE - Distribution of Organisms and their Sensitivity. Total Positive – 70 Samples

ORGANISMS	AMP	GM	CO	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
CONS[4]	1	2		3		1	2		2	2
ECOLI[27]	1	18	3	23	4	8	1	2	14	20
KLEBSIELLA[22]	1	15	4	19	2	5	2	3	4	17
NFGNB[11]		2	2	7	2	6		1	3	8
COLIFORMS[2]		1							1	1
ENTEROCOCCUS[1]										1
CITROBACTER[3]		2		1		1			1	2

E.coli is the predominant organism grown in urine culture 38.57% (27/70). It is sensitive to ciprofloxacin 85.18% (23/27) followed by amikacin 74.07% (20/27), ceftriaxone 51.85% and gentamicin 66.6%.

Klebsiella is an equally common organism causing UTI (31.2%). It is sensitive to ciprofloxacin (86.36%) followed by amikacin (77.27%) and gentamicin (68.18%).

NFGNB is the next common organism (15.71%). It is relatively resistant bacteria compared to other organisms grown in urine culture. It is sensitive to amikacin (72.72%), ciprofloxacin (63.63%) and norfloxacin (54.54%).

CONS, Citrobacter, coliforms and enterococcus are the other organisms grown in urine culture.

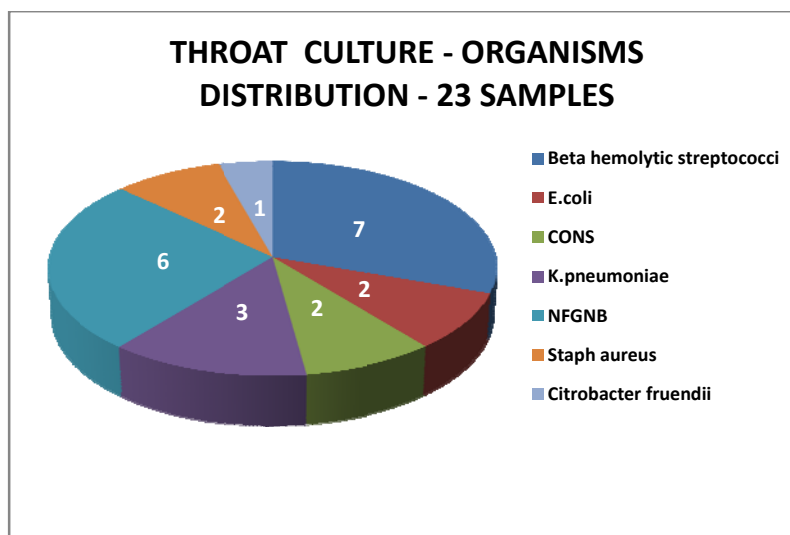
THROAT CULTURE

No of samples-23

- Culture positive - 23
- No growth - 0
- Contaminated - nil

Throat culture positive – 23 Samples

S.No.	Organisms	No. of samples	Percentage
1	Beta hemolytic streptococci	7	30.43%
2	E.coli	2	8.69%
3	CONS	2	8.69%
4	K.pneumoniae	3	13.04%
5	NFGNB	6	26.08%
6	Staph aureus	2	8.69%
7	Citrobacter fruendii	1	4.34%



THROAT SWAB CULTURE AND SENSITIVITY

Total number of positive culture – 23 Samples

Organisms	AMP	GM	DOXY	CIP	CEF	NOR	CLOX	ERY	CEFTRI	AMIK
CONS[2]	2	1	2	2			2		1	2
Ecoli[2]		1		2	1	1			1	2
Klebsiella[3]		1		1						1
NFGNB[6]		2	2	3		1			1	3
St.aureus[2]			1	1			2		1	
Citrobacter[1]			1	1		1				
Beta Hemolytic Streptococci[7]	3		2	4	3		3	5	1	

BACTERIOLOGICAL PROFILE OF THROAT CULTURE

Beta hemolytic streptococci is the most common organism isolated (30.43%) followed by NFGNB (26.08%), E.coli, CONS and staph aureus.

Beta hemolytic streptococci is highly susceptible to erythromycin (71.42%) followed by ciprofloxacin (57.14%). Ampicillin is also effective against it (42.85%).

NFGNB is the next common organism isolated. It is equally sensitive to amikacin and ciprofloxacin (50%) followed by genatamicin and doxycycline (33.33%).

Klebsiella in throat culture is highly resistant to all antibiotics. It is moderately sensitive to amikacin, ciprofloxacin and gentamicin (33.33%).

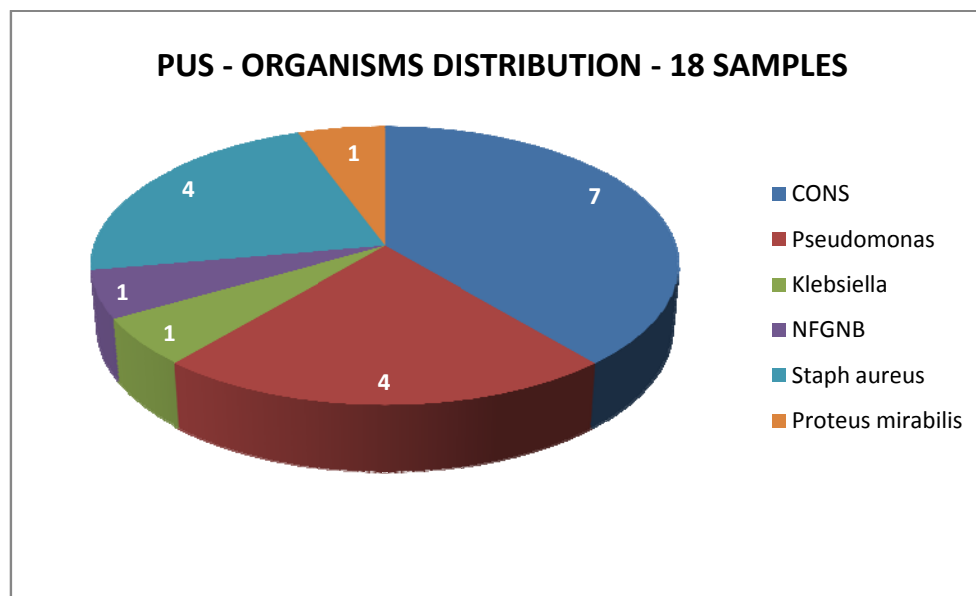
PUS CULTURE

No of samples-18

- Culture +ve - 18
- No growth - NIL
- Contaminated - NIL

CULTURE +VE-18 SAMPLES

S.No.	Organisms	No. of samples	Percentage
1	CONS	7	38.89%
2	Pseudomonas	4	22.22%
3	Klebsiella Oxytoca	1	5.55%
4	NFGNB	1	5.55%
5	Staph aureus	4	22.22%
6	Proteus mirabilis	1	5.55%



PUS CULTURE AND SENSITIVITY PATTERNS

Total number of positive samples -18

ORGANISMS	AMP	GM	ERY	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
CONS[7]	2	1	2	6	2		5	4	2	5
Klebsiella[1]		1		1					1	1
NFGNB[1]		1		1	1	1			1	1
St.aureus[4]			1	1			2		1	
Pseudomonas[4]		2		2			2		1	2
Proteus[1]		1				1			1	1

BACTERIOLOGICAL PROFILE OF PUS CULTURE

CONS is the predominant organism grown in pus. It is highly sensitive to ciprofloxacin (85.71%), cloxacillin (71.42%) and amikacin (71.42%). Cephalexin is also effective (57.14%).

Staph aureus and pseudomonas are the other common organisms isolated from pus. Staph aureus is sensitive to cloxacillin (50%) than cephalosporins and erythromycin. Pseudomonas is sensitive to gentamicin and ciprofloxacin (50%).

Proteus, klebsiella and NFGNB are the other common organisms grown in pus.

MOTION

- Total samples-9
- Negative -5

Culture +ve-4

- Shigella -3
- K.oxytoca-1

MOTION CULTURE AND SENSITIVITY PATTERN

Total Positive Samples – 4

Organisms	AMP	GM	CO	CIP	CEF	NOR	NA	CEPH	CEFTRI	AMIK
Shigella (3)		2		3		1		2	2	2
Klebsiella (1)				1		1				1

Shigella is the predominant organism (75%) in motion. It is highly sensitive to Ciprofloxacin (100%), Gentamicin and Amikacin (66.66%).

CSF culture

CSF culture was taken from eight suspected cases of meningitis, (Headache, altered sensorium) but all proved to be culture negative.

SENSITIVE PATTERNS OF COMMON ORGANISMS ISOLATED FROM DIFFERENT SITES

In 5 cases simultaneous cultures from skin infection, blood and urine were taken. Of these no cases had same organisms grown from all 3 sites.

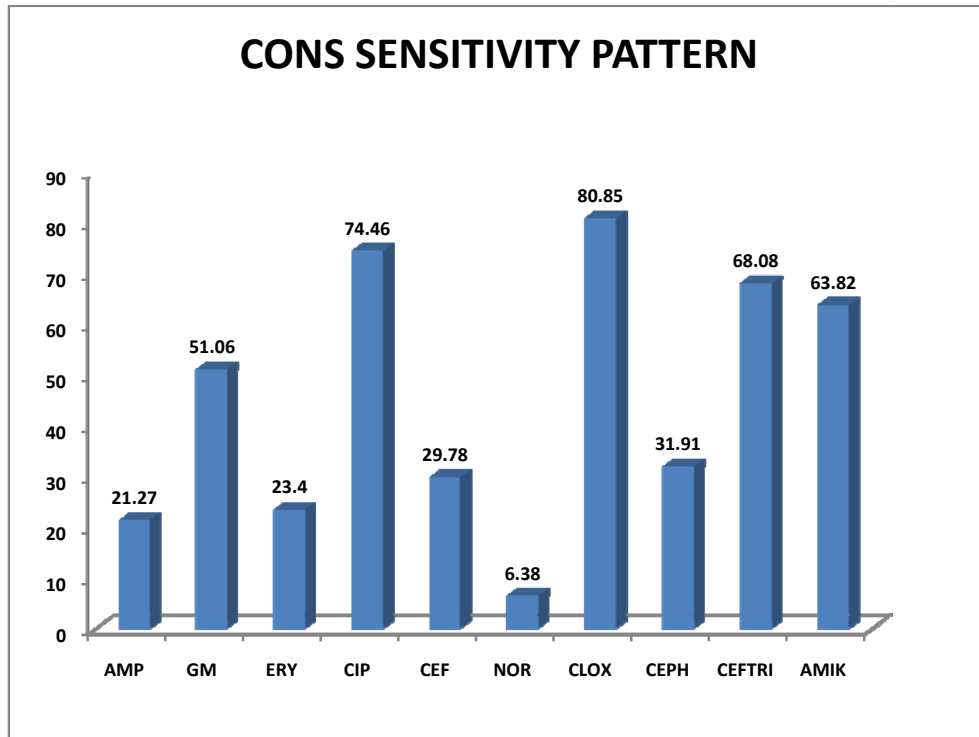
Simultaneous blood, urine culture was done in 59 cases. Of these six cases had same organisms grown in blood and urine.

This implies that multiple infection is common in leukemics. A total of 19 organisms were resistant to all the common antibiotics. Staph aureus (5), klebsiella (4), NFGNB (4), pseudomonas (3) E.coli (2), CONS (1) are the organisms distribution for these 19 resistant bacteria.

From the above data which was collected, the sensitivity pattern of the same organisms isolated from different sites were analysed.

CONS SENSITIVITY PATTERN

SAMPLE	AMP	GM	ERY	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
Blood [34]	5	20	7	24	12	2	29	11	27	21
Urine[4]	1	2	-	3	-	1	2	-	2	2
Throat[2]	2	1	2	2	-	-	2	-	1	2
Pus[7]	2	1	2	6	2	-	5	4	2	5
Total (47)	10	24	11	35	14	3	38	15	32	30
Percentage	21.27	51.06	23.40	74.46	29.78	6.38	80.85	31.91	68.08	63.82



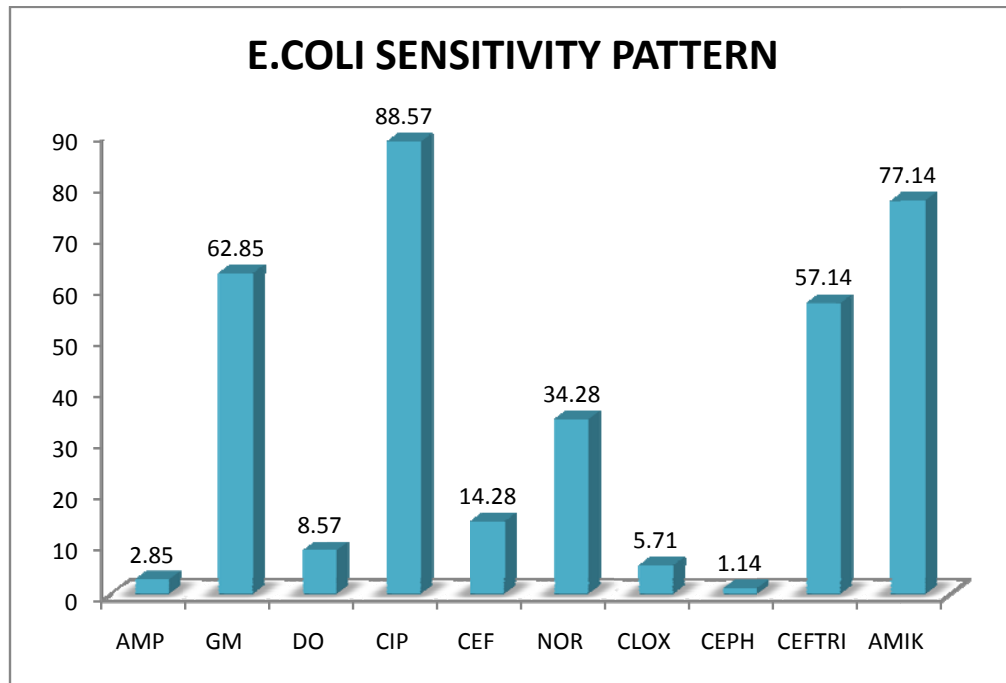
Cloxacillin is preferred to ampicillin for CONS $p = 0.002$ (chi Square – 10.068).

Amikacin and ceftriaxone (3rd generation cephalosporins) are equally effective $p = 0.9$ (insignificant).

The sensitive pattern of CONS grown from different sites is similar. Alternatively CONS isolated from pus alone is highly sensitive to ciprofloxacin (85.71%).

E.COLI SENSITIVITY PATTERN

SAMPLE	AMP	GM	DO	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
Blood [3]	-	1	-	3		2	-	-	3	3
Urine[27]	1	18	3	23	4	8	2	2	14	20
Throat[2]	-	1	-	2	1	1	-	-	1	2
Motion(3)	-	2	-	3	-	1	-	2	2	2
Total (35)	1	22	3	31	5	12	2	4	20	27
Percentage	2.85	62.85	8.57	88.57	14.28	34.28	5.71	1.14	57.14	77.14



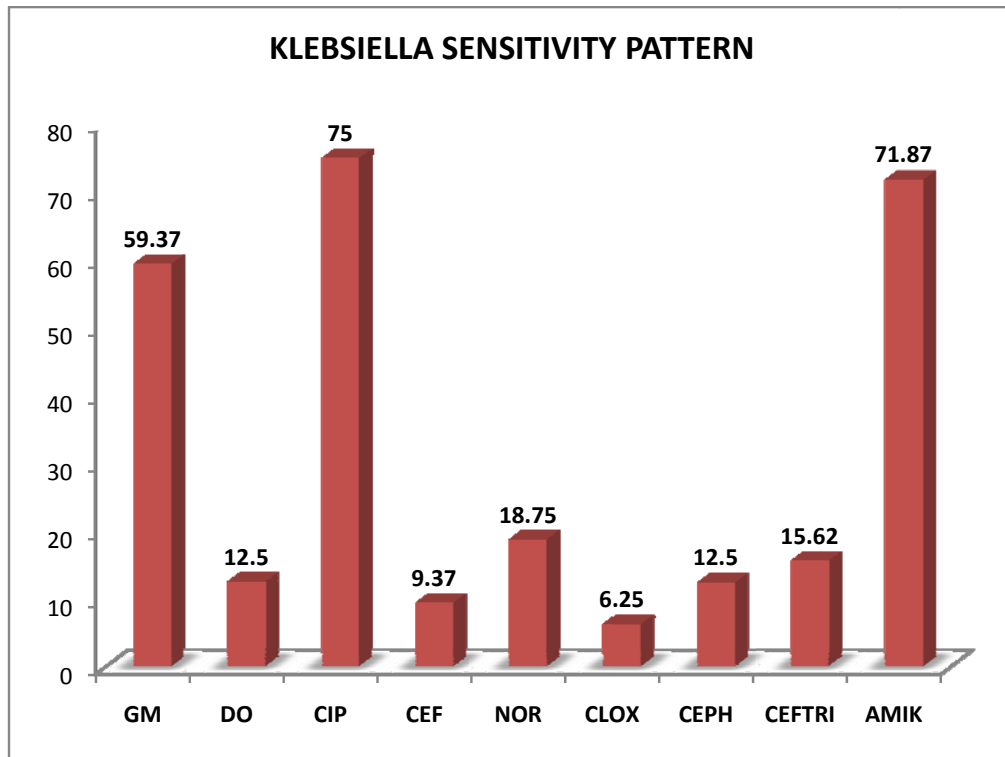
Ciprofloxacin is preferred to norfloxacin $p=0.034$ (Chi Square – 4.48).

Amikacin is preferred to cefotaxime, cephalixin, (Cephalosporins) $p < 0.001$ (10.95).

E.coli is uniformly sensitive to ciprofloxacin and amikacin irrespective of the site of sample collection.

KLEBSIELLA SENSITIVITY PATTERN

SAMPLE	AMP	GM	DO	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
Blood [5]	1	2		2	1	-	-	1	1	3
Urine [22]	1	15	4	19	2	5	2	3	4	17
Throat [3]	-	1	-	1	-	-	-	-	-	1
Pus [1]	-	1	-	1	-	-	-	-	1	1
Motion(1)	-	-	-	1	-	1	-	-	-	1
Total (32)	2	19	4	24	3	6	2	4	5	23
Percentage	6.25	59.37	12.5	75	9.37	18.75	6.25	12.5	15.62	71.87



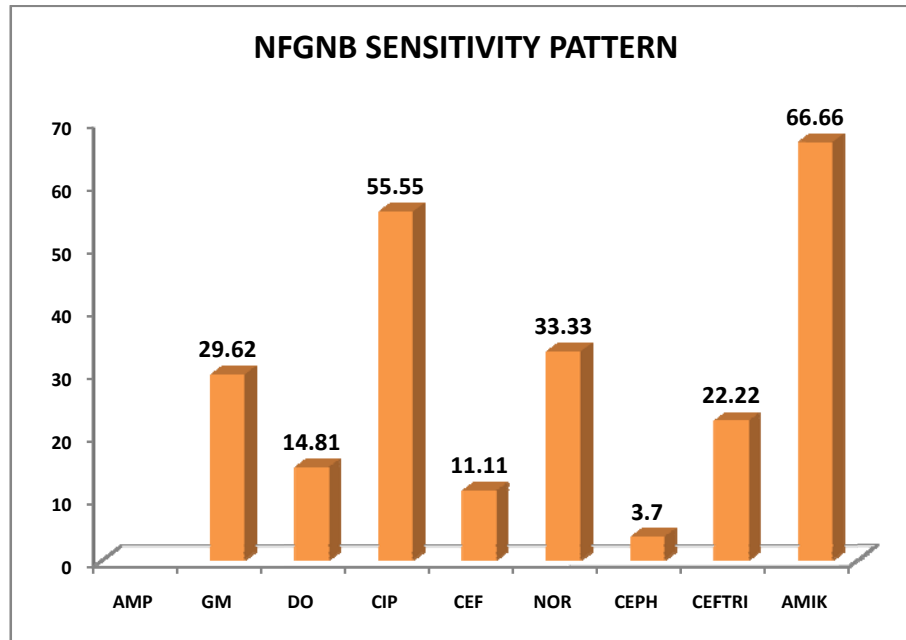
Ciprofloxacin is preferred to norfloxacin $p = 0.011$ (6.43)

Amikacin and Gentamicin are Equally effective $p = 0.779$ (0.079).

Klebsiella is moderately resistant to the common antibiotics. It is uniformly sensitive to ciprofloxacin and amikacin.

NFGNB SENSITIVITY PATTERN

SAMPLE	AMP	GM	DO	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
Blood (9)	-	3	-	4	-	1	-	-	1	6
Urine (11)	-	2	2	7	2	6	-	1	3	8
Throat (6)	-	2	2	3		1	-	-	1	3
Pus (1)	-	1	-	1	1	1	-	-	1	1
Total (27)	-	8	4	15	3	9	-	1	6	18
Percentage	-	29.62	14.81	55.55	11.11	33.33	-	3.7	22.22	66.66



Ciprofloxacin and norfloxacin are equally effective $p = 0.438$
(0.602)

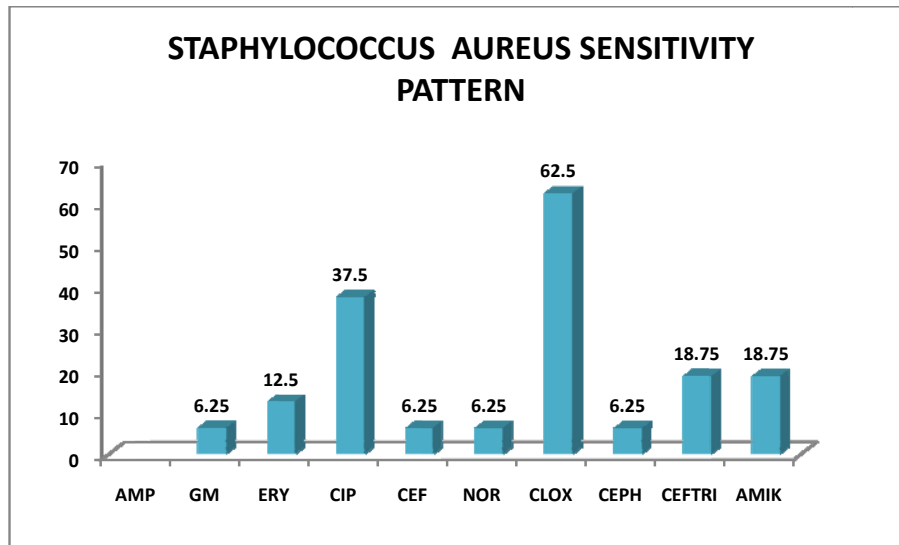
Amikacin and Gentamicin are equally effective $p = 0.167$ (1.91)

Also Ciprofloxacin and Amikacin are equally effective.

NFGNB is uniformly resistant organism irrespective of the site
of isolation.

STAPHYLOCOCCUS AUREUS SENSITIVITY PATTERN

SAMPLE	AMP	GM	ERY	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
Blood [10]		1		4	1	1	6	1	1	3
Throat [2]			1	1			2		1	
Pus[4]			1	1			2		1	
Total (16)		1	2	6	1	1	10	1	3	3
Percentage		6.25	12.5	37.5	6.25	6.25	62.5	6.25	18.75	18.75



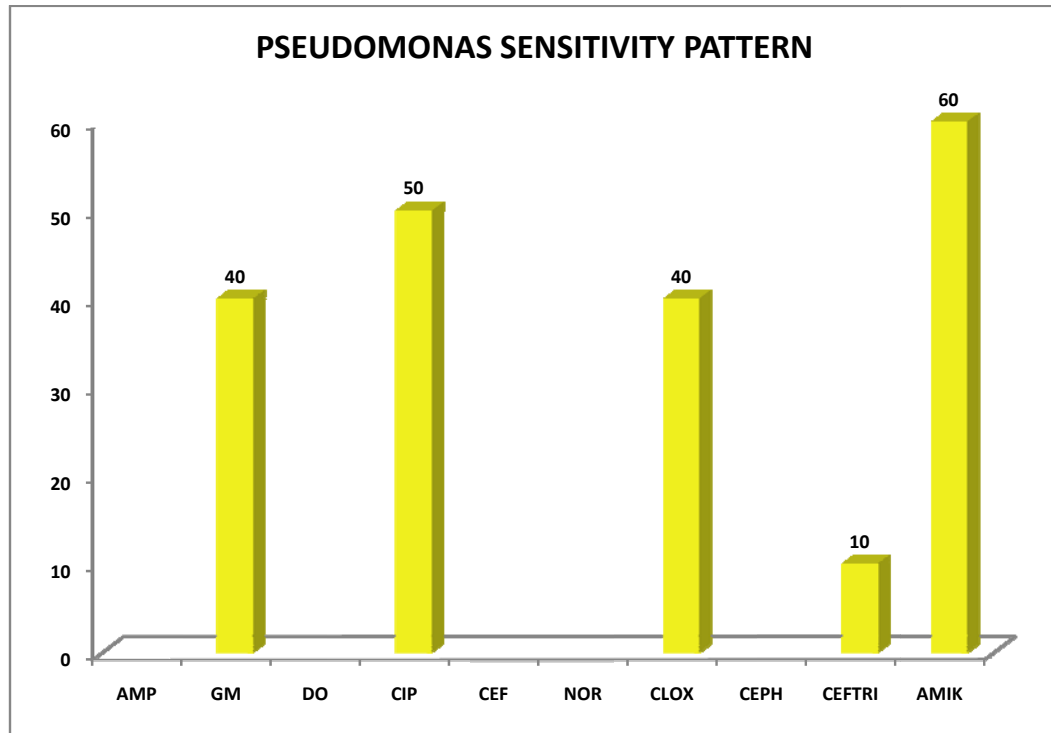
Cloxacillin is preferred over Ampicillin $p = 0.014$ (6.09)

Ciprofloxacin is the next alternative antibiotic.

Staph aureus is sensitive to cloxacillin than to any other antibiotic.

PSEUDOMONAS SENSITIVITY PATTERN

SAMPLE	AMP	GM	DO	CIP	CEF	NOR	CLOX	CEPH	CEFTRI	AMIK
Blood [6]	-	2	-	3	-	-	2	-	-	4
Pus[4]	-	2	-	2	-	-	2	-	1	2
Total (10)	-	4	-	5	-	-	4	-	1	6
Percentage	-	40	-	50	-	-	40	-	10	60



Amikacin, ciprofloxacin and Gentamicin are equally effective.

P – 0.897 (0.016).

P value of these antibiotics when compared with each other is insignificant.

Multi drug resistant pseudomonas is not a major threat from the analyzed samples in our patients.

DISCUSSION

CONS is the predominant organism isolated from our study while staph aureus and mycobacteria are the common organisms from Gopalnath study¹.

CONS is usually resistant to many antibiotic as per the study of Gopinath et al but in our study it is highly susceptible to common antibiotics.

The other commonest organism isolated were staph aureus, E.coli, klebsiella in both the studies.

Antibiotics chosen for empirical therapy of episodes of febrile neutropenia must be active against the majority of Gram-negative pathogens, as these bacteria are associated with high mortality. However, with the emergence of viridans streptococci as significant pathogens in immunocompromised patients, the ideal empirical regimen should also have activity against these organisms²².

In our study CONS is the predominant organism in blood, e.coli and klebsiella in urine. This is similar to Srivastava et al¹⁸ study where gram-negative bacteria causing UTI were mainly *Escherichia*

coli and *Klebsiella pneumoniae*, while gram-negative bacteria causing RTI were mainly *Klebsiella pneumonia*.

Ashour et al also reported the evolution of imipenem-resistant gram-negative strains in Egypt. Mortality rates were higher in leukemic patients with nosocomial *Pseudomonas* infections than any other bacterial infections. Policies restricting antibiotic consumption should be implemented to avoid the evolution of newer generations of antibiotic resistant-pathogens.

Similar reports from sheriff et al is that skin infections and blood stream infections were mainly Coagulase-negative staphylococcus (CONS) and *S. aureus*, whereas bacteria causing throat and respiratory infections were mainly alpha-hemolytic streptococci and CONS.

Our study shows CONS as highly sensitive and *s.aureus* and *klebsiella* as resistant bacteria against the common antibiotics but sheriff reported vancomycin- and linezolid-resistant *S. aureus* in Egypt. and Newer generation quinolones (moxifloxacin and gatifloxacin) were more active than older quinolones (ciprofloxacin and ofloxacin) against *S. aureus* and CNS, suggesting the use of newer generation quinolones in the prophylaxis of cancer patients.

Gopalnath et al¹ had done study in North East Indian population where ciprofloxacin resistance is very common. But in our study ciprofloxacin is the most effective antibiotic for gram negative infections and next to cloxacillin for gram positive infections.

Majority of gram negative isolates (E.coli, klebsiella) are sensitive to amikacin in both studies staph aureus is resistant to amikacin but sensitive to cloxacillin unlike Gopalnath's study similar suggestions were made by previous investigations also^{24,25}.

Streptococcus viridans, staph aureus, E.coli, klebsiella are the common organisms from Deepa Anirudhan et al²⁹ study but Group B streptococcus, NFGNB are common isolates of our study.

LIMITATIONS

1. Viral, fungal, anaerobic and some bacteria which require special media cannot be isolated in this study due to limited resources.
2. Newer antibiotics susceptibility were not included in this study due to financial constraints.
3. Correlation between type of organisms with stage of chemotherapy and blood counts could not be ascertained.

CONCLUSION

1. Leukemic children are more prone to various infections due to poor immunity. The predominant micro organisms in leukemic patients are :
 - a. coagulase negative staphylococcus aureus in blood.
 - b. E.Coli and Klebsiella in urine
 - c. Beta hemolytic streptococci and non fermentative gram negative bacilli in throat swab.
 - d. CONS, Staphylococcus aureus and pseudomonas in pus.
 - e. Klebsiella, Shigella (NFGNB) in motion.
2. Susceptibility of organisms to antibiotic is nearly similar irrespective of the source of isolation.
3. From the sensitive pattern of organisms studied CONS is highly susceptible to cloxacillin and ciprofloxacin. E.coli is susceptible to amikacin and ciprofloxacin. Klebsiella is relatively resistant to our common antibiotics and sensitive to ciprofloxacin and amikacin. NFGNB is more resistant organism and sensitive to amikacin and ciprofloxacin. Staphylococcus aureus is sensitive to cloxacillin. Pseudomonas is sensitive to amikacin and ciprofloxacin.

4. The incidence of multi drug resistant organisms in leukemics is common in leukemic patients (mainly *Staphylococcus aureus*, NFGNB and *klebsiella*).
5. The highest isolation of CONS *E.coli*, *Klebsiella pneumonia*, Non fermentative gram negative bacilli, *S. aureus*, and *Pseudomonas aeruginosa* indicates that special attention should be given to these bacteria during treatment when there is any febrile episode in leukemia patients.
6. Some of the patients where no pathogen could be detected may have some anaerobic bacteria for which special efforts should be made.
7. Ciprofloxacin is the universal antibiotic active against both gram positive and negative bacteria.
8. Amikacin / gentamicin is more effective than ceftriaxone for gram negative infections. Cloxacillin is the most effective antibiotic for gram positive infections.

RECOMMENDATIONS

1. Strict aseptic precautions should be adhered while examining them or doing procedures as they are highly vulnerable to infections.
2. Separate ward with air filters with frequent fumigation is essential
3. Antibiotic treatment should be entirely based on culture & sensitivity reports.
4. Empirical treatment is preferably avoided for fear of multidrug resistance, antibiotic failure / irrational use and drug induced complications.
5. In case of resource poor settings if at all empirical treatment should be started then a combination of cloxacillin (for gram positive organisms) and amikacin / ciprofloxacin has to be started.

MACCONKEY'S MEDIUM



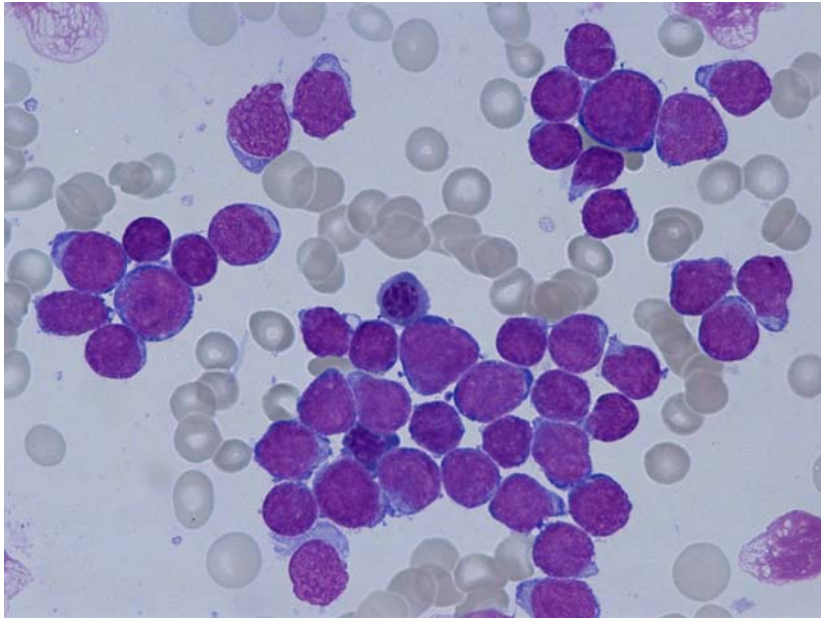
LACTOSE FERMENTERS



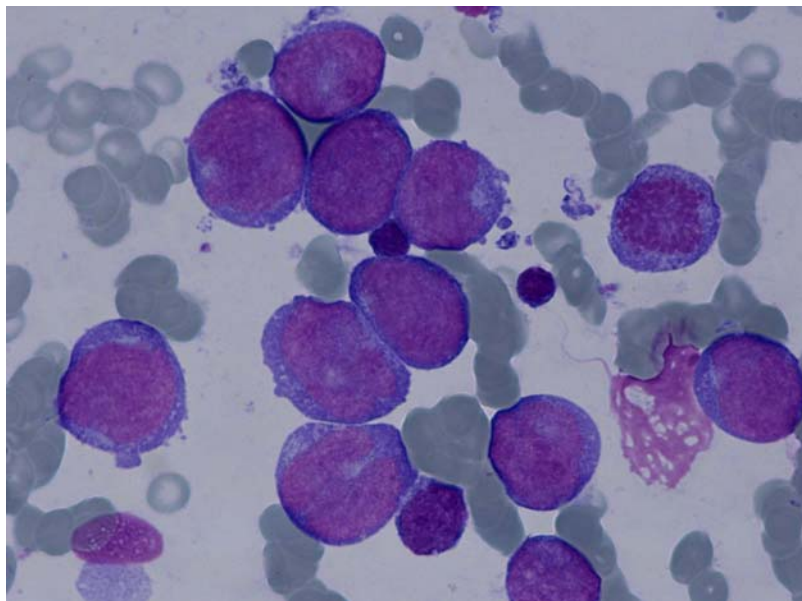
BLOOD CULTURE BOTTLES



ALL



AML



S.No	Name	Age	Sex	IP No	SYMPTOMS									SOURCE OF SAMPLE COLLECTED							Positive Growth	ORGANISM ISOLATED					
					Fever	Dysuria	Sore Throat	Oral Ulcers	Skin Ulcer	Deep Abscess (Internal)	Lymph Nodes enlargement	IV Site Abscess	Pus	Loose Stools	Blood (B)	Urine (U)	Throat (T)	Skin (S)	Motion (M)	CSF(C)		Blood	Urine	Throat	Skin	Motion	CSF
1	Boopathi	5	M	35216	Y	N	N	N	N	N	N	N	Y	N	+	+	-	-	-	-	B,U	C	K	-	-	-	-
2	Balakrishnan	8	M	36238	Y	N	N	N	N	N	N	N	Y	N	+	+	-	-	-	-	B,U	C	N	-	-	-	-
3	Mounaselvaraj	7	M	23412	Y	N	Y	N	N	N	N	Y	Y	N	+	+	-	-	-	-	B,U	E	NG	-	-	-	-
4	Santhoshkumar	9	M	12421	Y	N	Y	N	N	Y	Y	N	N	N	+	-	+	-	-	-	B,T	S	-	B	-	-	-
5	Manikandan	4	M	26721	Y	N	N	N	N	N	N	N	N	N	-	-	+	-	-	-	T	-	-	C	-	-	-
6	Veeramani	6	M	34216	Y	N	N	Y	Y	N	N	Y	Y	N	-	-	+	+	-	+	T,S	-	-	N	-	-	NG
7	Sneha	4	F	12416	Y	Y	Y	Y	Y	N	Y	N	N	N	+	+	-	+	-	-	S	NG	NG	-	S	-	-
8	Prithivi	7	M	32165	Y	N	N	N	N	N	N	N	N	N	+	+	-	-	-	-	B,U	C	E	-	-	-	-
9	Karuppasamy	6	M	42861	Y	N	N	Y	Y	N	N	N	N	Y	+	-	-	-	+	-	B,M	C	-	-	-	NG	-
10	Praveen	10	M	68216	Y	N	N	Y	Y	N	N	N	N	N	+	-	-	+	+	-	S,T	-	-	N	C	-	-
11	Avinash	6	M	52136	Y	N	N	Y	Y	N	Y	N	N	N	+	+	+	+	-	-	B,T, S	C	NG	N	P	-	-
12	Sivadharaani	4	M	48216	Y	N	Y	N	N	N	N	N	N	N	+	+	-	-	-	+	B,U	C	E	-	-	-	NG
13	Rabiya	6	F	56142	Y	N	N	N	N	N	Y	N	N	Y	+	+	-	-	+	-	B,T	P	-	B	-	SH	-
14	Balamurugan	8	M	63126	Y	N	Y	N	N	N	N	N	N	N	-	-	+	-	-	-	T	-	-	N	-	-	-
15	Sakthivel	9	M	62111	Y	N	N	Y	Y	N	N	Y	N	N	+	+	-	+	-	-	B,U,S	C	E	-	C	-	-
16	Logesh	4	M	44526	Y	N	N	Y	Y	N	Y	N	N	N	+	+	+	-	-	-		NG	NG	-	-	-	-
17	Karuppasamy	8	M	48261	N	N	Y	Y	Y	N	Y	N	N	N	+	+	-	+	-	-	B,U,S	S	K	-	C	-	-
18	Lokesh	5	M	43216	Y	N	N	N	N	N	N	N	N	N	+	+	-	-	-	-		NG	NG	-	-	-	-
19	Santhosh	6	M	55216	Y	N	Y	N	N	N	N	Y	N	Y	+	+	-	-	+	+	B,U,M,R	S	-	-	-	SH	NG
20	Karuppasamy	4	M	23125	Y	N	N	N	N	N	N	N	N	N	-	-	+	+	-	-	S,T	-	-	B	S	-	-
21	Avinash	6	M	52678	Y	N	N	Y	Y	N	Y	Y	N	N	+	+	+	-	-	-	T	-	NG	N	-	-	-
22	Lokesh	5	M	58241	N	Y	Y	N	N	N	N	N	N	N	+	+	-	-	-	-	U	NG	E	-	-	-	-
23	Nivedha	6	F	57216	Y	Y	N	N	N	N	N	Y	N	N	+	+	-	-	-	-	B,U	E	NG	-	-	-	-
24	Shiva	5	M	50129	Y	N	Y	N	N	N	Y	N	N	N	+	+	-	-	-	-	U	NG	K	-	-	-	-
25	Koodalingam	10	M	51738	Y	N	N	Y	Y	Y	N	N	N	N	+	+	-	-	-	+	B	K	NG	-	-	-	NG
26	Lokesh	5	M	53487	Y	N	Y	N	N	N	Y	N	N	N	+	+	-	+	-	-	S	NG	C	-	C	-	-
27	Santhosh	6	M	65297	Y	Y	N	N	N	N	Y	N	N	Y	+	+	-	-	+	-	B	C	-	-	-	NG	-
28	Agalya	5	F	63712	N	N	N	Y	Y	N	Y	N	N	N	-	-	+	-	-	-	T	-	C	C	-	-	-
29	Siva	5	M	65129	Y	N	N	N	N	N	N	N	N	N	+	-	-	-	-	-	B	C	NG	-	-	-	-
30	Karuppasamy	8	M	67839	Y	N	N	N	N	N	N	N	N	N	+	+	-	-	-	-	U	NG	C	-	-	-	-
31	Sivadharaani	5	F	64196	N	N	N	Y	Y	N	Y	N	N	N	+	+	-	+	-	-	B,U,S	C	-	-	C	-	-
32	Nishanthi	4	F	69127	Y	N	N	N	N	N	N	N	N	N	-	-	+	-	-	-	T	-	-	B	-	-	-
33	Jegadeesh	7	M	76921	N	Y	N	Y	Y	N	Y	N	N	N	-	+	-	-	-	+	U	-	NG	-	-	-	NG
34	Nivetha	6	F	74262	Y	N	N	N	N	N	N	Y	N	Y	-	+	-	-	+	-	B,M	NG	NG	-	-	K	-

S.No	Name	Age	Sex	IP No	SYMPTOMS									SOURCE OF SAMPLE COLLECTED							Positive Growth	ORGANISM ISOLATED					
					Fever	Dysuria	Sore Throat	Oral Ulcers	Skin Ulcer	Deep Abscess (Internal)	Lymph Nodes enlargement	IV Site Abscess	Pus	Loose Stools	Blood (B)	Urine (U)	Throat (T)	Skin (S)	Motion (M)	CSF(C)		Blood	Urine	Throat	Skin	Motion	CSF
35	Koodalingam	10	M	72164	N	N	N	N	N	N	Y	N	N	N	+	+	-	+	-	-	S	NG	C	-	P	-	-
36	Santhosh	8	M	78412	Y	N	N	Y	Y	N	N	N	N	N	+	+	-	-	-	-	B,U	C	-	-	-	-	-
37	Siva	7	M	77216	N	N	N	N	N	N	N	N	N	N	-	+	+	-	-	-	U,T	-	C	B	-	-	-
38	Sneha	6	F	73412	Y	N	N	N	N	N	Y	N	N	N	+	+	-	-	-	-	B,U	C	-	-	-	-	-
39	Nandhini	4	F	79412	Y	N	N	N	N	N	N	Y	N	N	-	-	-	+	+	+	S	-	-	-	C	NG	NG
40	Santhosh Kumar	11	M	78627	N	Y	N	Y	Y	N	Y	N	N	Y	-	+	-	+	-	-		-	C	-	-	-	-
41	Rajavarshika	4	M	77428	Y	N	N	N	N	N	N	N	N	N	+	+	-	-	-	-	B,U	C	NG	-	-	-	-
42	Naveen Raja	10	M	76421	N	N	N	N	N	N	N	N	N	N	+	+	-	-	-	-		NG	NG	-	-	-	-
43	Chandrasekar	12	M	71426	Y	N	N	Y	Y	N	N	N	N	N	+	-	+	-	-	-	B,T	N	-	N	-	-	-
44	Veeramani	6	M	73489	Y	N	N	Y	Y	N	Y	N	N	N	+	-	+	-	-	-	T	NG	-	C	-	-	-
45	Boomiraj	11	M	72162	Y	N	N	N	N	N	N	N	N	N	+	-	-	+	-	-	B,T,S	C	E	E	S	-	-
46	Balakrishnan	10	M	74126	Y	N	N	N	N	N	Y	N	N	N	+	+	-	-	-	-	B	C	K	-	-	-	-
47	Vishwabarathi	9	M	75138	N	Y	N	N	N	N	N	N	N	N	-	+	+	-	-	-	U	-	-	-	-	-	-
48	Praveen	6	M	79216	Y	Y	N	N	N	N	Y	N	N	N	+	-	-	-	-	-	B,U,T	E	E	N	-	-	-
49	Martin vijay	10	M	78123	Y	N	N	N	N	N	N	N	N	Y	+	+	-	+	+	-	B,S,M	K	K	-	C	SH	
50	Vignesh	6	M	77489	N	Y	N	N	N	N	Y	N	N	N	-	+	+	-	-	-	U	-	NG	-	-	-	-
51	Pappammal	6	F	76279	Y	Y	Y	Y	Y	N	Y	N	N	N	+	+	+	-	-	+	B,U,T	E	-	B	-	-	NG
52	Sneha	4	F	79218	Y	N	N	Y	Y	N	N	N	N	N	+	-	-	-	-	-	B,U,T	K	N	E	-	-	-
53	Ajith	11	M	77421	Y	N	N	N	N	N	Y	N	N	N	+	+	-	-	-	-	B	NG	NG	-	-	-	-
54	Akalya	4	F	79826	N	N	N	N	N	N	Y	N	N	Y	+	+	-	+	+	-	B,U,S	C	K	-	C	NG	-
55	Sivadarani	5	F	84216	Y	Y	N	N	N	N	N	N	N	N	+	-	+	-	-	-	B	N	N	-	-	-	-
56	Nisha	3	F	87839	Y	Y	N	Y	Y	N	N	N	N	N	+	+	-	-	-	-	B,U	NG	E	C	-	-	-
57	Sivadarani	4	F	82126	Y	N	N	Y	Y	N	N	N	N	N	+	+	+	+	-	+	B,U	-	K	-	P	-	NG
58	Abi	2	F	62164	Y	N	N	N	N	N	Y	N	N	N	+	+	-	-	-	-	B,T	N	E	B	-	-	-
59	Riyaz Ahmad	11	M	85412	Y	N	N	N	N	N	N	N	N	N	+	+	-	-	-	-	B,U,S	E	N	-	-	-	-
60	Vignesh	9	M	72142	Y	N	N	N	N	N	Y	N	N	N	+	+	-	-	-	-	B,U,T	K	E	-	-	-	-
61	Priya	4	F	34216	Y	N	N	N	N	N	N	N	N	N	+	+	-	+	-	-	B,U	E	E	-	C	-	-
62	Gopiprasath	10	M	54213	Y	N	N	N	N	N	Y	N	N	N	+	+	-	-	-	-	B,U	N	-	-	-	-	-
63	Simran	5	F	46212	Y	N	N	N	N	N	N	N	N	N	+	+	-	-	-	-	B,U,S	E	K	-	-	-	-
64	Kowsalya	4	F	64126	Y	Y	N	N	N	N	Y	N	N	N	+	+	-	-	-	-	B,U	E		-	-	-	-

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